REMARKS

Claims 82-92 are currently pending in the application and are rejected under 35 U.S.C. 102(e) and obviousness-type double patenting. Reconsideration and withdrawal of the rejections are requested.

Objections To The Specification

The Examiner has objected to the title and abstract of the invention as they do not mention the claimed subject matter and, in particular, do not mention antibodies. Applicant has amended the title and abstract to reflect the claimed subject matter.

Applicant has amended the specification to update the status of applications to which priority has been claimed.

Objections To The Claims

The Examiner has objected to Claim 90 in view of the misspelling of the term "interleukin". Claim 90 has been amended to correct the error.

The Examiner has objected to Claims 82 and 85-87 as having awkward phrasing and has suggested that the claims be amended to recite "osteoprotegerin binding protein of SEQ ID NO:39". Applicant has amended the claims accordingly.

Claim Rejections

In the present Office Action, Claims 82-92 stand rejected under 35 U.S.C. 102(e) as being anticipated by Gorman *et al.* (U.S. Patent No. 6,242,586, hereafter the "'586 patent") for the reasons of record as set forth in the Office Action of May 18, 2005.

Claim 82 recites a "human monoclonal antibody or fragment thereof which binds specifically to an osteoprotegerin binding protein of SEQ ID NO:39, wherein the antibody or fragment thereof inhibits osteoclast formation." The Examiner argues that the '586 patent discloses methods for producing human monoclonal antibodies and that these teachings are supported in the priority application (U.S. Serial No. 60/032,846). The Examiner further argues that the 499E9 polypeptide disclosed in the '586 patent is

identical to mouse osteoprotegerin binding protein (hereafter "OPGbp") and is 84.1% identical at the amino acid sequence level to human OPGbp (SEQ ID NO:39 of the present application). On p. 4 of the Office Action of May 18, 2005, the Examiner argues that the '586 patent anticipates the claimed human monoclonal antibodies as follows:

> The instant claims recite the functional limitation that the claimed human monoclonal antibodies inhibit osteoclast formation. It is noted that the disclosure of Gorman *et al.* [the '586 patent] do (sic) not teach the 499E9 protein as being involved in the bone remodeling process. However, given that the sequences of human and mouse osteoprotegerin binding proteins are substantially identical, it is reasonable that antibodies that specifically bind mouse osteoprotegerin binding protein as taught by Gorman *et al.* will also bind human osteoprotegerin binding protein. It is also reasonable that these same antibodies that cross-react with human osteoprotegerin binding protein will inhibit osteoclast formation, especially in absence of evidence to the contrary. As such, even though Gorman *et al.* do not teach the functional limitation of inhibiting osteoclast formation, the structure of the antibodies taught by Gorman *et al.* are substantially identical to those recited in the instant claim

"A claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference" *Celeritas Techs. Ltd v. Rockwell Int'l Corp.* 47 USPQ2d 1516, 1522 (Fed. Cir. 1998). A prior art reference may anticipate even when claim limitations are not expressly found in that reference, but are nonetheless inherent in it. See e.g., *Atlas Powder Co. v. IRECO Inc.*, 51 USPQ2d 1943 (Fed. Cir. 1999); *Titanium Metals Corp. v. Banner* 227 USPQ 773 (Fed. Cir. 1985). "Inherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Oelrich* 212 USPQ 323, 326 (CCPA 1981).

The Examiner states that the claims in the present application recite the functional limitation of inhibiting osteoclast formation but concedes that the disclosure of Gorman *et al.* "does not teach the functional limitation of inhibiting osteoclast formation." Thus, the claims are not expressly anticipated by the '586 patent. Moreover, the Examiner has not offered any reasoning or evidence that the claims are inherently anticipated by the '586 patent. As indicated above, the Examiner relies on the high degree of similarity in amino acid sequence between murine and human OPGbp to argue that it is "reasonable" for antibodies which specifically bind murine OPGbp to also bind, or cross-react with, human OPGbp and that it would be "reasonable" that the same cross-reacting antibodies would also inhibit osteoclast formation. However, the

argument that such antibodies would reasonably result in view of the teachings of the '586 patent falls far short of the standard for inherent anticipation where such antibodies must necessarily result from the teachings of the '586 patent. No evidence has been provided to suggest that the same antibodies which specifically bind murine OGPbp and cross-react with human OPGbp would necessarily inhibit osteoclast formation. The Examiner's further argument that the structure of the antibodies taught by Gorman *et al.* (the '586 patent) are substantially identical to those recited in the instant claims and are therefore functionally the same is wholly unsupported. No evidence has been presented to indicate that antibodies which specifically bind to murine OPGbp and cross-react with human OPGbp would necessarily be structurally and functionally identical to human monoclonal antibodies which specifically bind human OPGbp.

In the Office Action of February 3, 2006, the Examiner alleges that antibodies raised against murine OPGbp as allegedly taught by the '586 patent would cross-react with human OPGbp due to the 84.1% identity between mouse and human OPGbp. It is also argued that the BB' and EF loop regions of murine and human OPGbp are highly similar and are identified in the application as peptide antigens for immunization, allegedly supporting the position that antibodies binding murine OPGbp would cross-react with human OPGbp. However, the Examiner's reliance on antibody cross-reactivity is not sufficient for anticipation. The claims recite a human antibody which specifically binds to human OPGbp and inhibits osteoclast formation, yet the argument that an antibody which binds murine OPbp and can cross-react with human OGPbp does not expressly or inherently disclose the claimed antibodies. No reasoning or evidence has been presented to show that an antibody which specifically binds murine OPGbp will necessarily bind specifically to human OPGbp and inhibit osteoclast formation.

In summary, the Examiner has failed to establish a *prima facie* case of anticipation based on the teachings of the '586 patent and the rejection should be withdrawn.

Claims 82-92 stand provisionally rejected under obviousness-type double patenting over Claims 2-9, 21 and 22 of co-pending U.S. Serial No. 10/180,648 (hereafter the "'648 application"), over Claims 1-50, 52 and 53-73 of co-pending U.S. Serial No. 10/408,901 (hereafter the "'901 application"), and over Claims 10-53 of

co-pending U.S. Serial No. 09/791,153 (hereafter the "'153 application") in view of Lonberg *et al.* (citation unknown). The Lonberg *et al.* reference was alleged to be made of record on form PTO-892 dated May 18, 2005 although no such reference is indicated therein. The '648, '901 and '153 applications disclose and claim certain OPGbp antibodies having the activity of inhibiting osteoclast formation and bone resorption. The Examiner has argued that the specific variable region sequences claimed in the '648 application "anticipate the claimed genus of human monoclonal antibodies that bind human OPGbp" (para. 11, p. 9 of the Office Action dated May 18, 2005). The claims cited in the '901 and '153 application also recite specific antibody sequences that bind human OPGbp and thus are included in the rejection for similar reasons.

"Obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly-owned patent when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by the patent" (MPEP section 804; *Eli Lilly & Co. v. Barr Labs., Inc.* 58 USPQ2d 1869 (Fed. Cir. 2001). A claim under examination is rejected as being not patentably distinct where it is anticipated by, or would have been obvious over, a claim in a separate application or patent, where the application(s) or patent(s) must have at least one common inventor and/or be commonly owned or assigned.

The '648, '901 and '153 applications cited in this rejection have priority dates of June 26, 2001, April 5, 2002 and February 23, 2000, respectively, all of which are later than the April 16, 1997 priority date of the present application. Since later filed disclosures claiming antibody species cannot anticipate or render obvious an earlier filed and claimed antibody genus encompassing the species, none of the claims the cited applications can be used to anticipate or render obvious any of the present claims. In addition, Issuance of the present application as a patent would not unjustly extend the term of exclusion since such a patent would have an expiration date earlier than any patent which would issue from any of the '648, '901 and '153 applications. Moreover, Examiner acknowledges at p. 10 of the present Office Action that this rejection has no effect on patentability:

> ...failure to distinguish the instant claims from the claims of the other applications and/or failure to file appropriate terminal disclaimers would not impede the allowance of the instant claims...

Given that the present obviousness-type double patenting rejection is not proper, it is not necessary for the Applicant to reply to the underlying arguments. In doing so, however, Applicant does not acquiesce to the rejection and reserves the right to respond to other obviousness-type double patenting rejections in this and other related applications. It is requested that the rejection be withdrawn.

Applicant acknowledges that the rejection of Claims 82, 83 and 85-92 under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,641,747 to Popoff *et al.* as evidenced by Yang *et al.* (Proc. Natl. Acad. Sci. USA 82, 7994-7998 (1985)) and PCT Publication No. 93/12227 (Lonberg *et al.*) has been withdrawn.

The Examiner states that additional co-pending applications that list William Boyle among the inventors were identified which allegedly claim subject matter "substantially identical to that claimed in the instant application", but was unable to find "any indication that applicant has discussed the potential for duplicative subject matter in these related cases" by citing the co-pending applications. Applicant has no obligation whatsoever to "discuss the potential for duplicative subject matter" in any cited co-pending application in the absence of any action properly rejecting claims on that basis. As discussed above, the provisional obviousness-type double patenting rejections based on several co-pending applications listing William Boyle among the inventors are moot as they have no effect on the patentability of the present claims.

CONCLUSION

Claims 82-92 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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